

GenCore version 4.5
Copyright (c) 1993 - 2000 CompuGen Ltd.

OM protein - protein search, using sw model

Run on: September 27, 2001, 16:43:31 ; Search time 16.74 seconds

(without alignments)
667.102 Million cell updates/sec

Title: US-09-483-543a-9

Perfect score: 1733

Sequence: 1 KKGAGNFDSEERSSWYGR.....SCCGXGLEVLPFGVRKGGXG 326

Scoring table: BLOSUM62

Searched: 93435 seqs, 34255486 residues

Total number of hits satisfying chosen parameters: 93435

Minimum DB seq length: 0

Maximum DB seq length: 200000000

Post-processing: Minimum Match 0%

Maximum Match 100%

Database : SwissProt_39:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	ID	Description
1	1612	93.0	304	1 CRK_MOUSE	Q64010 mus musculu
2	1605	92.6	304	1 CRK_RAT	Q63768 rattus norv
3	1588	91.6	304	1 CRK_HUMAN	P46108 homo sapien
4	1379.5	79.6	305	1 CRK_CHICK	Q04929 gallus gall
5	1315	75.9	296	1 CRK_XENLA	P87378 xenopus lae
6	917.5	52.9	303	1 CRKL_HUMAN	P46109 homo sapien
7	911.5	52.6	303	1 CRKL_MOUSE	P47941 mus musculu
8	818.5	47.2	440	1 GAGC_AYISC	P05433 avian sarco
9	642.5	37.1	271	1 CRK_DROME	Q9XYM0 drosophila
10	257	14.8	217	1 GRAP_HUMAN	Q13588 homo sapien
11	236	13.6	211	1 DRK_DROME	Q08012 drosophila
12	224	12.9	217	1 GRB2_HUMAN	P29314 homo sapien
13	224	12.9	217	1 GRB2_MOUSE	Q60631 mus musculu
14	218	12.6	217	1 GRB2_CHICK	Q07883 gallus gall
15	214	12.3	217	1 GRB2_XENLA	P87379 xenopus lae
16	202	11.7	228	1 SEM5_CAEL	P29335 caenorhabdi
17	184	10.6	1291	1 PIG1_BOVIN	P08487 bos taurus
18	178	10.3	1290	1 PIG1_HUMAN	P19174 homo sapien
19	177	10.2	1290	1 PIG1_RAT	P10666 rattus norv
20	174.5	10.1	322	1 GRP2_MOUSE	Q89100 m grb2-rela
21	174	10.0	845	1 VAV_HUMAN	P15498 homo sapien
22	173	10.0	843	1 VAV_RAT	P54100 rattus norv
23	167	9.6	845	1 VAV_MOUSE	P27870 mus musculu
24	159.5	9.2	847	1 VAV3_HUMAN	Q9UKW4 homo sapien
25	158.5	9.1	330	1 GRP2_HUMAN	Q75791 h grb2-rela
26	157	9.1	520	1 ITSN_HUMAN	Q15811 homo sapien
27	155.5	9.0	847	1 VAV3_MOUSE	Q91068 mus musculu
28	154.5	8.9	848	1 VAV2_HUMAN	P52735 homo sapien
29	151	8.7	1168	1 MYSC_ACACA	P10569 acanthamoeb
30	150	8.7	960	1 PLGI_DROME	P31007 drosophila
31	148.5	8.6	868	1 VAV2_MOUSE	Q60992 mus musculu
32	148.5	8.6	1113	1 MYSD_DICDI	P34109 dictyostell
33	147	8.5	1044	1 GTPA_BOVIN	P09851 bos taurus

34	146.5	8.5	1038	1 GTPA_RAT	P50904 rattus norv
35	146	8.4	946	1 RHG4_HUMAN	P98171 homo sapien
36	144.5	8.3	1047	1 GTPA_HUMAN	P20936 homo sapien
37	142	8.2	450	1 CSK_CHICK	P41239 gallus gall
38	139	8.0	359	1 YKA7_CAEL	P34258 caenorhabdi
39	139	8.0	1196	1 ABIL1_CAEL	P03949 caenorhabdi
40	138.5	8.0	505	1 SRK1_SPOLA	P42686 spongilla 1
41	138.5	8.0	1265	1 PI62_RAT	P24135 rattus norv
42	138	8.0	583	1 SHC_HUMAN	P29353 homo sapien
43	137.5	7.9	578	1 SHC_MOUSE	P98083 mus musculu
44	136	7.8	450	1 CSK_HUMAN	P41240 homo sapien
45	134	7.7	450	1 CSK_MOUSE	P41241 mus musculu

ALIGNMENTS

```

RESULT 1
ID CRK_MOUSE STANDARD; PRT; 304 AA.
AC Q64010;
DT 01-NOV-1997 (rel. 35, Created)
DT 01-NOV-1997 (rel. 35, Last sequence update)
DT 15-JUL-1999 (rel. 38, Last annotation update)
DE PROTO-ONCOGENE C-CRK (P38) (ADAPTER MOLECULE CRK).
GN CRK OR CRKO.
OS Mus musculus (Mouse).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Mus.
OX NCBI_TaxID=10090;
RN [1]
RP SEQUENCE FROM N.A.
RX TISSUE=Liver;
RC MEDLINE=94239744; PubMed=8183562;
RA Ogawa S., Toyoshima H., Kozutsumi H., Hagiwara K., Sakai R.,
RA Tanaka T., Hirano N., Mano H., Yazaki Y., Hirai H.;
RT "The C-terminal SH3 domain of the mouse c-Crk protein negatively
RT regulates tyrosine-phosphorylation of Crk associated p130 in rat 3Y1
RT cells.";
RL Oncogene 9:1669-1678(1994).
RN [2]
RP X-RAY CRYSTALLOGRAPHY (1.5 ANGSTROMS) OF 134-190.
RX MEDLINE=95253821; PubMed=7735837;
RA Wu X., Knudsen B., Feller S.M., Zheng J., Sali A., Cowburn D.,
RA Hanafusa H., Kuriyan J.;
RT "Structural basis for the specific interaction of lysine-containing
RT proline-rich peptides with the N-terminal SH3 domain of c-Crk.";
RL Structure 3:215-226(1995).
RN [3]
RP X-RAY CRYSTALLOGRAPHY (2.5 ANGSTROMS) OF 133-191.
RX MEDLINE=99069628; PubMed=9851931;
RA Nguyen J.T., Turk C.W., Cohen F.E., Zuckermann R.N., Lim W.A.;
RT "Exploiting the basis of proline recognition by SH3 and WW domains:
RT design of N-substituted inhibitors.";
RL Science 282:2088-2092(1998).
CC -I- FUNCTION: THE CRK-I AND CRK-II FORMS DIFFER IN THEIR BIOLOGICAL
CC ACTIVITIES. CRK-II HAS LESS TRANSFORMING ACTIVITY THAN CRK-I. BOTH
CC CRK-I AND CRK-II BIND TO MANY OF TYROSINE-PHOSPHORYLATED PROTEINS
CC THAT BIND TO GRB2.
CC -I- ALTERNATIVE PRODUCTS: 2 ISOFORMS; CRK-I AND CRK-II (SHOWN HERE);
CC ARE PRODUCED BY ALTERNATIVE SPLICING. THE CRK-I FORM LACKS THE
CC LAST 100 RESIDUES.
CC -I- TISSUE SPECIFICITY: UBIQUITOUS.
CC -I- DOMAIN: THE C-TERMINAL SH3 DOMAIN FUNCTION AS A NEGATIVE MODULATOR
CC FOR TRANSFORMATION AND THE N-TERMINAL SH3 DOMAIN APPEARS TO
CC FUNCTION AS A POSITIVE REGULATOR FOR TRANSFORMATION (BY
CC SIMILARITY).
CC -I- SIMILARITY: CONTAINS 1 SH2 DOMAIN.
CC -I- SIMILARITY: CONTAINS 2 SH3 DOMAINS.
CC -----
CC This SWISS-PROT entry is copyright. It is produced through a collaboration
CC between the Swiss Institute of Bioinformatics and the EMBL outstation-
CC the European Bioinformatics Institute.. There are no restrictions on its

```


QY 305 DFS 307
111
Db 302 DFS 304

RESULT 3
ID CRK_HUMAN STANDARD; PRT; 304 AA.

AC P46108;
DT 01-NOV-1995 (Rel. 32, Created)
DT 01-NOV-1995 (Rel. 32, Last sequence update)
DE 01-OCT-2000 (Rel. 40, Last annotation update)
DE PROTO-ONCOGENE C-CRK (P38) (ADAPTER MOLECULE CRK).
GN CRK.
OS Homo sapiens (Human).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Primates; Catarrhini; Homnidae; Homo.
OX NCBI_TaxID=9606;
RN [1]
RP SEQUENCE FROM N.A.
RC TISSUE=Embryonic lung, and Placenta;
RX MEDLINE=9234347; PubMed=1630456;
RA Matsuda M., Tanaka S., Nagata S., Kojima A., Kurata T., Shibuya M.;
RT "Two species of human CRK cDNA encode proteins with distinct
biological activities."
RL Mol. Cell. Biol. 12:3482-3489(1992).
RN [2]
RP SEQUENCE FROM N.A.
RX MEDLINE=93390962; PubMed=8378094;
RA Floretos T., Heisterkamp N., Groffen J., Benjes S., Morris C.;
RT "CRK proto-oncogene maps to human chromosome band 17p13."
RL Oncogene 8:2853-2855(1993).
CC -1- FUNCTION: THE CRK-I AND CRK-II FORMS DIFFER IN THEIR BIOLOGICAL
ACTIVITIES. CRK-II HAS LESS TRANSFORMING ACTIVITY THAN CRK-I. BOTH
CRK-I AND CRK-II BIND TO MANY OF TYROSINE-PHOSPHORYLATED PROTEINS
THAT BIND TO GRB2.
CC -1- ALTERNATIVE PRODUCTS: 2 ISOFORMS; CRK-I AND CRK-II (SHOWN HERE);
ARE PRODUCED BY ALTERNATIVE SPLICING. THE CRK-I FORM LACKS THE
LAST 100 RESIDUES.
CC -1- DOMAIN: THE C-TERMINAL SH3 DOMAIN FUNCTION AS A NEGATIVE MODULATOR
FOR TRANSFORMATION AND THE N-TERMINAL SH3 DOMAIN APPEARS TO
FUNCTION AS A POSITIVE REGULATOR FOR TRANSFORMATION
CC -1- PPM: PHOSPHORYLATION OF CRK-II (40 KDA) GIVES RISE TO A 42 KDA
FORM.
CC -1- SIMILARITY: CONTAINS 1 SH2 DOMAIN.
CC -1- SIMILARITY: CONTAINS 2 SH3 DOMAINS.

CC This SWISS-PROT entry is copyright. It is produced through a collaboration
between the Swiss Institute of Bioinformatics and the EMBL outstation -
the European Bioinformatics Institute. There are no restrictions on its
use by non-profit institutions as long as its content is in no way
modified and this statement is not removed. Usage by and for commercial
entities requires a license agreement (See <http://www.isb-sib.ch/announce/>
or send an email to license@isb-sib.ch).

CC EMBL; D10656; BAA01505.1; -;
DR EMBL; S65701; AAB28213.1; -;
DR HSSP; Q64010; ICRB.
DR SWISS-2DPAGE; P46108; HUMAN.
DR MIM; 164762; -;
DR InterPro; IPR000980; -;
DR InterPro; IPR001452; -;
DR Pfam; PF00017; SH2; 1.
DR Pfam; PF00018; SH3; 1.
DR PRINTS; PRO0401; SH2DOMAIN.
DR PRINTS; PRO0452; SH3DOMAIN.
DR PROSITE; PSS0001; SH2; 1.
DR PROSITE; PSS0002; SH3; 1.
DR Proto-oncogene; SH2 domain; SH3 domain; Alternative splicing;
KW Phosphorylation.
FT DOMAIN 13 118 SH2.
FT DOMAIN 132 192 SH3.
FT DOMAIN 256 296 SH3.

FT VARSPIC 205 304 MISSING (IN ISOFORM CRK-I).
SQ SEQUENCE 304 AA; 33872 MW; D7A83ED1FC0EBC CRK64;
Query Match 91.6%; Score 1588; DR 1; Length 304;
Best local Similarity 98.7%; Pred. No. 2.6e-107;
Matches 299; Conservative 1; Mismatches 3; Indels 0; Gaps 0;

QY 5 AGNFDEERSWYWGRLSRQEAVALLOQGRHGFVLRDSTSPGQVYLSVNSRVSHTY 64
|||||
Db 2 AGNFDEERSWYWGRLSRQEAVALLOQGRHGFVLRDSTSPGQVYLSVNSRVSHTY 61
|||||
QY 65 INSSGPRPPYPSPAOPPPGVSPSRIRIDQEPDSLPALLEFYKHYLDPTTLIPVARS 124
|||||
Db 62 INSSGPRPPYPSPAOPPPGVSPSRIRIDQEPDSLPALLEFYKHYLDPTTLIPVARS 121
|||||
QY 125 ROSSGYLRQEEAEYRALFDENGDEEDLPFKGDILRIKRPPEQWMAEDSGKRG 184
|||||
Db 122 ROSSGYLRQEEAEYRALFDENGDEEDLPFKGDILRIKRPPEQWMAEDSGKRG 181
|||||
QY 185 IVPYVEKYRPASASVSALIGNQEGSHPOPLGPEPGYAPSVNTPLPNLQNGPIYAR 244
|||||
Db 182 IVPYVEKYRPASASVSALIGNQEGSHPOPLGPEPGYAPSVNTPLPNLQNGPIYAR 241
|||||
QY 245 VIGKRVPMAYDKTALALEVGLVYKTKIVSGQEGECNGKRGHPETHVRLDQNPDE 304
|||||
Db 242 VIGKRVPMAYDKTALALEVGLVYKTKIVSGQEGECNGKRGHPETHVRLDQNPDE 301
|||||

QY 305 DFS 307
111
Db 302 DFS 304

RESULT 4
ID CRK_CHICK STANDARD; PRT; 305 AA.

AC Q04929;
DT 01-NOV-1995 (Rel. 32, Created)
DT 01-NOV-1995 (Rel. 32, Last sequence update)
DT 01-NOV-1995 (Rel. 32, Last annotation update)
DE PROTO-ONCOGENE C-CRK (P38).
GN CRK.
OS Gallus gallus (Chicken).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;
OC Gallus.
OX NCBI_TaxID=9031;
RN [1]
RP SEQUENCE FROM N.A.
RX MEDLINE=93041379; PubMed=1329926;
RA Reichman C.T., Mayer B.J., Khawer S., Hanafusa H.;
RT "The product of the cellular crk gene consists primarily of SH2 and
SH3 regions."
RL Cell Growth Differ. 3:451-460(1992).
CC -1- SIMILARITY: CONTAINS 1 SH2 DOMAIN.
CC -1- SIMILARITY: CONTAINS 2 SH3 DOMAINS.

CC This SWISS-PROT entry is copyright. It is produced through a collaboration
between the Swiss Institute of Bioinformatics and the EMBL outstation -
the European Bioinformatics Institute. There are no restrictions on its
use by non-profit institutions as long as its content is in no way
modified and this statement is not removed. Usage by and for commercial
entities requires a license agreement (See <http://www.isb-sib.ch/announce/>
or send an email to license@isb-sib.ch).

CC EMBL; I08168; AAA49001.1; -;
DR HSSP; Q64010; ICRB.
DR InterPro; IPR000980; -;
DR InterPro; IPR001452; -;
DR Pfam; PF00017; SH2; 1.
DR Pfam; PF00018; SH3; 1.
DR PRINTS; PRO0401; SH2DOMAIN.
DR PRINTS; PRO0452; SH3DOMAIN.

RA Mayer B.J., Hamaguchi M., Hanafusa H.;
 RT "A novel viral oncogene with structural similarity to phospholipase
 C-";
 RL Nature 332:272-275(1998).
 CC -1- SIMILARITY: CONTAINS 1 SH2 DOMAIN.
 CC -1- SIMILARITY: CONTAINS 1 SH3 DOMAIN.
 CC -----
 CC This SWISS-PROT entry is copyright. It is produced through a collaboration
 CC between the Swiss Institute of Bioinformatics and the EMBL outstation-
 CC the European Bioinformatics Institute. There are no restrictions on its
 CC use by non-profit institutions as long as its content is in no way
 CC modified and this statement is not removed. Usage by and for commercial
 CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>
 CC or send an email to license@isb-sib.ch).
 CC -----
 DR EMBL: Y00302; CA68407.1; -;
 DR PIR: A29851; A29851.
 DR PIR: B29851; TVEV10.
 DR PIR: S00872; S00872.
 DR HSSP: Q64010; 1CRP.
 DR InterPro: IPR000980; -;
 DR InterPro: IPR001452; -;
 DR Pfam: PF00017; SH2; 1.
 DR Pfam: PF00018; SH3; 1.
 DR PRINTS: PR00401; SH2DOMAIN.
 DR PRINTS: PR00452; SH3DOMAIN.
 DR PROSITE: PS50001; SH2; 1.
 DR PROSITE: PS50002; SH3; 1.
 DR PROSITE: PS50002; SH3; 1.
 KM Oncogene: Polyprotein SH3 domain; SH2 domain.
 FT DOMAIN 1 208 GAG.
 FT DOMAIN 209 437 CRK.
 FT DOMAIN 438 440 GAG.
 FT DOMAIN 439 354 SH2.
 FT DOMAIN 368 428 SH3.
 SQ SEQUENCE 440 AA; 47176 MW; 0DB5438628982AC CRC64;

Query Match 47.2%; Score 818.5; DB 1; Length 440;
 Best Local Similarity 77.3%; Pred. No. 7.5e-52;
 Matches 157; Conservative 16; Mismatches 29; Indels 1; Gaps 1;

QY 5 AGNFDSEBSWTGRLSRQEAVALLOGRHGVLYRDSSTSGDYLVSVSENSRVSHYI 64
 DB 237 AGGFDSDSDRSGWYGRSLSRDAVSLLOGRHGVLYRDSSTSGDYLVSVSENSRVSHYI 296
 QY 65 INSSGPPVPSPAPOP-PRGVSPSRRLRGDOFDSLPLALFEYKTHYIDTTLIEPVAR 123
 DB 297 VNSLIGRAGGRAGGEGFAGLMPTRLIGDQYFDSLPLEYKTHYIDTTLIEPVSR 356
 QY 124 SRQSGVILRQEEAEYVRLAFNGNDEBDLPKKGDLIRNDKPEQWMNNAEDSGKRG 183
 DB 357 SRQSGVILRQEEAEYVRLAFNGNDEBDLPKKGDLIRNDKPEQWMNNAEDMDGKRG 416
 QY 184 MIPVYVEKYPASASVSLIGG 206
 DB 417 MIPVYVEKYPASASVSLTGG 439

RESULT 9
 CRK_DROME
 ID CRK_DROME STANDARD; PRT; 271 AA.
 AC 09XIM0;
 DT 01-OCT-2000 (Rel. 40, Created)
 DT 01-OCT-2000 (Rel. 40, Last sequence update)
 DT 01-OCT-2000 (Rel. 40, Last annotation update)
 DE ADAPTER MOLECULE CRK.
 GN CRK OR CG1587.
 OS Drosophila melanogaster (Fruit fly).
 OC Eukaryota; Metazoa; Arthropoda; Tracheata; Hexapoda; Insecta;
 OC Pterygota; Neoptera; Endopterygota; Diptera; Brachycera; Muscomorpha;
 OC Ephydroidea; Drosophilidae; Drosophila.
 OX NCBI_TaxId=7227;
 RN [1]

RP SEQUENCE FROM N.A. AND CHARACTERIZATION.
 RC TISSUE=Embryo;
 RX MEDLINE=99173888; PubMed=10072777;
 RA Galletta B.J., Niu X.-P., Erickson M.R., Abmayr S.M.;
 RT "Identification of a Drosophila homologue to vertebrate Crk by
 RT interaction with MBC";
 RL Gene 228:243-252(1999).
 RN [2]
 RP SEQUENCE FROM N.A.
 RC STRAIN=BERKELEY;
 RX MEDLINE=20196006; PubMed=10731132;
 RA Adams M.D., Celisner S.E., Holt R.A., Evans C.A., Gocayne J.D.,
 RA Amanatides P.G., Scherer S.E., Li P.W., Hoskins R.A., Galle R.F.,
 RA George R.A., Lewis S.E., Richards S., Ashburner M., Henderson S.N.,
 RA Sutton G.G., Wortman J.R., Yandell M.D., Zhang Q., Chen L.X.,
 RA Brandon R.C., Rogers Y.-H.C., Blazey R.G., Champe M., Peiffer B.D.,
 RA Wan K.H., Doyle C., Baxter E.G., Helt G., Nelson C.R., Miklos G.L.G.,
 RA Abril J.F., Agbayani A., An H.-J., Andrews-Pfannkoch C., Baldwin D.,
 RA Ballew R.M., Basu A., Baxendale J., Bayraktaroglu L., Beasley E.M.,
 RA Beeson K.Y., Benos P.V., Bernan B.P., Bhandari D., Bolshakov S.,
 RA Borokova D., Botchan M.R., Bouck J., Brokstein P., Brotler P.,
 RA Burlis K.C., Busam D.A., Butler H., Cadien E., Center A., Chandra I.,
 RA Cherry J.M., Cawley S., Dahlke C., Davenport L.B., Davies P.,
 RA de Pablos B., Delcher A., Deng Z., Mays A.D., Dew I., Dietz S.M.,
 RA Dodson K., Doup L.E., Downes M., Dugan-Rocha S., Dunkov B.C., Dunn P.,
 RA Durbin K.J., Evangelista C.C., Ferraz C., Ferreira S., Fleischmann W.,
 RA Foster C., Gabrielian A.E., Garg N.S., Gelbart W.M., Glasser K.,
 RA Glodex A., Gong F., Gorrell J.H., Gu Z., Guan P., Harris M.,
 RA Harris N.L., Harvey D., Helman T.J., Hernandez J., Houck J.,
 RA Hostin D., Houston K.A., Howland T.J., Wei M.-H., Idegam C.,
 RA Jaitani M., Kalush F., Karpen G.H., Ke Z., Kennison J.A., Ketchum K.A.,
 RA Kimmel B.E., Kodira C.D., Kraft C., Kravitz S., Kulp D., Lai Z.,
 RA Lasko P., Lei Y., Levitsky A.A., Li J., Li Z., Liang Y., Lin X.,
 RA Liu X., Mattei B., McIntosh T.C., McLeod M.P., McPherson D.,
 RA Merkulov G., Milshina N.V., Mobarry C., Morris J., Mosnelli A.,
 RA Mount S.M., Moy M., Murphy B., Murphy L., Muzny D.M., Nelson D.L.,
 RA Nelson D.R., Nelson K.A., Nixon K., Nusskern D.R., Paclet J.M.,
 RA Palazzolo M., Pittman G.S., Pan S., Pollard J., Puri V., Reese M.G.,
 RA Reinert K., Remington K., Saunders R.D.C., Scheefer F., Shen H.,
 RA Shue B.C., Siden-Kiamos I., Simpson M., Skupski M.P., Smith T.,
 RA Spier E., Spradling A.C., Stapleton M., Strong R., Sun E.,
 RA Svirskas R., Tector C., Turner R., Venter E., Wang A.H., Wang X.,
 RA Wang Z.-Y., Wassarman D.A., Weinstock G.M., Weissenbach J.,
 RA Williams S.M., Woodage T., Worley K.C., Wu D., Yang S., Yao Q.A.,
 RA Ye J., Yeh R.-F., Zaveri J.S., Zhan M., Zhang G., Zhao Q., Zheng L.,
 RA Zheng X.H., Zhong F.N., Zhong W., Zhou X., Zhu S., Zhu X., Smith H.O.,
 RA Gibbs R.A., Myers E.W., Rubin G.M., Venter J.C.;
 RT "The genome sequence of Drosophila melanogaster";
 RL Science 287:2185-2195(2000).
 CC -1- FUNCTION: ADAPTER PROTEIN WHICH INTERACTS WITH C-TERMINAL PORTION
 CC OF MBC, HOMOLOG OF HUMAN DOCK180. MAY PLAY A ROLE IN CELLULAR
 CC PROCESSES THROUGHOUT DEVELOPMENT.
 CC -1- TISSUE SPECIFICITY: EMBRYONIC ZYGOTIC EXPRESSION IS SEEN IN
 CC INVAGINATING PRESUMPTIVE MESODERM AND ECTODERMALLY DERIVED TISSUES
 CC DURING GASTROULATION. AT STAGE 8, EXPRESSION IS ALSO SEEN IN
 CC ANTERIOR AND POSTERIOR MIDGUT AND CEPHALIC FURROW. BY STAGE 9,
 CC EXPRESSION IS HIGHEST IN VISCERAL MESODERM OF ANTERIOR AND
 CC POSTERIOR MIDGUT, VENTRAL NERVE CORD AND SOMATIC MESODERM.
 CC -1- DEVELOPMENTAL STAGE: EXPRESSED BOTH MATERNALLY AND ZYGOTICALLY
 CC THROUGHOUT EMBRYOGENESIS, DECLINES DURING LARVAL STAGES AND
 CC REAPPEARS DURING POPULATION.
 CC -1- SIMILARITY: CONTAINS 1 SH2 DOMAIN.
 CC -1- SIMILARITY: CONTAINS 2 SH3 DOMAINS.
 CC -----
 CC This SWISS-PROT entry is copyright. It is produced through a collaboration
 CC between the Swiss Institute of Bioinformatics and the EMBL outstation-
 CC the European Bioinformatics Institute. There are no restrictions on its
 CC use by non-profit institutions as long as its content is in no way
 CC modified and this statement is not removed. Usage by and for commercial
 CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>
 CC or send an email to license@isb-sib.ch).
 CC -----
 DR EMBL: AE003844; AAF59362.1; -;

```

DR EMBL: AF112976; AAD28428.1; -.
DR HSSP: Q64010; 1CKA.
DR FlyBase: FBgn0024811; Crk.
DR InterPro: IPR000980; -.
DR InterPro: IPR001452; -.
DR Pfam: PF00017; SH2; 1.
DR Pfam: PF00018; SH3; 1.
DR PRINTS: PR00401; SH2DOMAIN.
DR PRINTS: PR00452; SH3DOMAIN.
DR PROSITE: PS50001; SH2; 1.
DR PROSITE: PS50002; SH3; 1.
DR SH2 domain; SH3 domain; Developmental protein.
FT DOMAIN 12 114 SH2.
FT DOMAIN 117 165 SH3.
FT DOMAIN 220 259 SH3.
SQ SEQUENCE 271 AA; 31205 MW; D1BAFEA3150932DC CRC64;

Query Match 37.1%; Score 642.5; DB 1; Length 271;
Best Local Similarity 43.8%; Pred. No. 1.8e-39;
Matches 133; Conservative 42; Mismatches 68; Indels 61; Gaps 6;

QY 8 FDSERSSWYMGRLSROEVALLOQGR-HGVFLVROSTSPGQYVLSVSENSVSHYIN 66
DB 4 FVSDRSNWTFFGPMRSODATEVLMNEREGVFLVROSNISAGDYVLCVREDTFVSNYIN 63
QY 67 SSGRRPVPVPPSPAPQPPGVSPSLRIGDQFDSLPALEFFKTHYLDTTLLIPVARSQ 126
DB 64 KVGQDQDIY-----YRIGDQSFQDNLKRLFTYTHYLDTPPLKRPACR--- 106
QY 127 GSGVILROEAEYRALPFDNGNDEEDLPKKGDILIRDKPEEOMWNAEDSECKRGMT 186
DB 107 -----REKVIKGFDEVGSDODDLPQRGSEVILYKDKEDQWMTARNSGKIGQIF 157
QY 187 VPYEYK-----RPASASVALIGQNEGSHPPPLGPERGPVPAQSVMPPLP 234
DB 158 VPIYQDIDTMDDEADIDKNPSISGSSNVESITL-----RTDLNKL- 200
QY 235 NLONGPIYARVIOKRVNAVYKDTALAEVGLVYKTKINVGOMEGECNGKRGHPTTH 294
DB 201 ----PAYARVKOSRVPNAYDKTALKLEIGDITKVTKTININGQMEGLNKGHPETH 255
QY 295 RLID 298
DB 256 EFVD 259

RESULT 10
GRAP_HUMAN STANDARD; PRT; 217 AA.
ID GRAP_HUMAN
AC Q13588;
DT 15-DEC-1998 (Rel. 37, Created)
DT 15-DEC-1998 (Rel. 37, Last sequence update)
DE 01-OCT-2000 (Rel. 40, Last annotation update)
DE GRB2-RELATED ADAPTOR PROTEIN.
GN GRAP.
OS Homo sapiens (Human).
OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Primates; Catarrhini; Hominiidae; Homo.
OX NCBI_TaxID=9606;
RN [1]
RP SEQUENCE FROM N.A.
RX MEDLINE=96218119; PubMed=8647802;
RA Feng G.-S., Ouyang Y.-B., Hu D.-P., Shi Z.-Q., Genz R., Ni J.;
RT "Grp is a novel SH3-SH2-SH3 adaptor protein that couples tyrosine
RT kinases to the Ras pathway.";
RT J. Biol. Chem. 271:12129-12132(1996).
CC -1- FUNCTION: COUPLES SIGNALS FROM RECEPTOR AND CYTOPLASMIC TYROSINE
CC KINASES TO THE RAS SIGNALING PATHWAY.
CC -1- SUBUNIT: ASSOCIATES THROUGH ITS SH2 DOMAIN WITH LIGAND-ACTIVATED
CC RECEPTORS FOR STEM CELL FACTOR (KIT) AND ERYTHROPOIETIN (EPOR).
CC ALSO FORMS A STABLE COMPLEX WITH THE BCR-ABL ONCOPROTEIN. GRAP IS
CC ASSOCIATED WITH THE RAS GUANINE NUCLEOTIDE EXCHANGE FACTOR SOS1,

```

```

CC CC PRIMARILY THROUGH ITS N-TERMINAL SH3 DOMAIN.
CC -1- SIMILARITY: CONTAINS 1 SH2 DOMAIN.
CC -1- SIMILARITY: CONTAINS 2 SH3 DOMAINS.
CC -1- SIMILARITY: BELONGS TO THE GRB2 / SEM-5 / DRK FAMILY.
CC -----
CC CC This SWISS-PROT entry is copyright. It is produced through a collaboration
CC between the Swiss Institute of Bioinformatics and the EMBL Outstation -
CC the European Bioinformatics Institute. There are no restrictions on its
CC use by non-profit institutions as long as its content is in no way
CC modified and this statement is not removed. Usage by and for commercial
CC entities requires a license agreement (see http://www.isb-sib.ch/announce/
CC or send an email to license@isb-sib.ch).
CC -----
CC CC EMBL: U52518; AAC50541.1; -.
CC DR MEM: 604330; -.
CC DR InterPro: IPR000980; -.
CC DR InterPro: IPR001452; -.
CC DR Pfam: PF00017; SH2; 1.
CC DR Pfam: PF00018; SH3; 2.
CC DR PRINTS: PR00452; SH3DOMAIN.
CC DR PROSITE: PS50001; SH2; 1.
CC DR PROSITE: PS50002; SH3; 2.
CC KW SH2 domain; SH3 domain.
CC FT DOMAIN 1 58 SH3.
CC FT DOMAIN 60 152 SH2.
CC FT DOMAIN 156 215 SH3.
CC SQ SEQUENCE 217 AA; 25336 MW; 09FEC2F3BAC0FAF8 CRC64;

Query Match 14.8%; Score 257; DB 1; Length 217;
Best Local Similarity 31.4%; Pred. No. 6.6e-12;
Matches 64; Conservative 40; Mismatches 54; Indels 46; Gaps 9;

QY 2 RGCAG---NFDSESSWYMGRLSROEVALLOQGRH-HGVFLVROSTSPGQYVLSVSE 56
DB 42 RVEGEFIPNNTYRKVPHMYSGRISRLAEELMKRNHLGFLIRESSSGEFSVSNY 101
QY 57 NSRVSHYII--NSSGRRPVPVPPSPAPQPPGVSPSLRIGDQFDSLPALEFFKTHYLD 114
DB 102 GQVOHFVKVLRASG-----KYFLMEKFNLSNLTVDYFR-----T 137
QY 115 TTLIEPVARSRGSGVILROE-----AEYRALPFDNGNDEEDLPKKGDILIRDK 167
DB 138 TT---IARKRQ---IFLREDEPLKSPACFAQAFDPSQSLSFRRGDIIEVLER 190
QY 168 PEEOMWNAEDSECKRGMTVPVYE 191
DB 191 PDPHMKGR-SCGRVGFPPRSTVQ 213

RESULT 11
DRK_DROME STANDARD; PRT; 211 AA.
ID DRK_DROME
AC O08012; Q9V605;
DT 01-FEB-1995 (Rel. 31, Created)
DT 01-FEB-1995 (Rel. 31, Last sequence update)
DE 01-OCT-2000 (Rel. 40, Last annotation update)
DE PROTEIN K(Sev)2B (SH2-SH3 ADAPTER PROTEIN DRK).
GN DRK OR E(Sev)2B OR CG6033.
OS Drosophila melanogaster (Fruit fly).
OC Eukaryota; Metazoa; Arthropoda; Tracheata; Hexapoda; Insecta;
OC Pterygota; Neoptera; Endopterygota; Diptera; Brachycera; Muscomorpha;
OC Ephydroidea; Drosophilidae; Drosophila.
OX NCBI_TaxID=7227;
RN [1]
RP SEQUENCE FROM N.A.
RX TISSUE=Eye;
RX MEDLINE=93214989; PubMed=8462097;
RA Simon M.A., Dodson G.S., Rubin G.M.;
RT "An SH3-SH2-SH3 protein is required for p21Ras1 activation and binds
RT to sevenless and Sos proteins in vitro.";
RT Cell 73:169-177(1993).
RN [2]

```

RP SEQUENCE FROM N.A.
RC TISSUE=Embryo;
RA MEDLINE=93214990; PubMed=8462098;
RA Olivier J.P., Raabe T., Henkemeyer M., Dickson B., Mbemalu G.,
RA Margolis B., Schlessinger J., Hafen E., Pawson T.;
RT "A Drosophila SH2-SH3 adaptor protein implicated in coupling the
RT sevenless tyrosine kinase to an activator of Ras granule nucleotide
RT exchange. Sos.";
RL Cell 73:1179-191(1993).
RN [3]
RP SEQUENCE FROM N.A.
RC STRAIN=BERKELEY;
RC MEDLINE=20196006; PubMed=10731132;
RA Adams M.D., Celniker S.E., Holt R.A., Evans C.A., Gocayne J.D.,
RA Amanatides P.G., Scherer S.E., Li P.W., Hoskins R.A., Galie R.F.,
RA George R.A., Lewis S.E., Richards S., Ashburner M., Henderson S.N.,
RA Sutton G.G., Wortman J.R., Yandell M.D., Zhang Q., Chen L.X.,
RA Brandon R.C., Rogers Y.-H.C., Blaise R.G., Champé M., Pfeiffer B.D.,
RA Wan K.H., Doyle C., Baxter E.G., Helt G., Nelson C.R., Miklos G.L.G.,
RA Abril J.F., Adabayani A., An H.-J., Andrews-Pfankuch C., Baldwin D.,
RA Ballew R.M., Basu A., Baxendale J., Bayraktaroglu L., Beasley E.M.,
RA Beeson K.Y., Benos P.V., Berman B.P., Bhandari D., Bolshakov S.,
RA Borokova D., Botchan M.R., Bouck J., Brokstein P., Brothier P.,
RA Burtis K.C., Busam D.A., Butler E., Cadieu E., Center A., Chandra I.,
RA Cherry J.M., Cawley S., Dahlke C., Davenport L.B., Davies P.,
RA de Pablos B., Delcher A., Deng Z., Mays A.D., Dew I., Dietz S.M.,
RA Dodson K., Doup I.E., Downes M., Dugan-Rocha S., Dunkov B.C., Dunn P.,
RA Durbin K.J., Evangelista C.C., Ferraz C., Ferlita S., Fleischmann W.,
RA Foster C., Gabrielian A.E., Gary N.S., Gelbart W.M., Glasser K.,
RA Glodde C., Gong F., Gorrell J.H., Gu Z., Guan P., Harris M.,
RA Harris N.L., Harvey D., Heiman T.J., Hernandez J.R., Houck J.,
RA Hostin D., Houston K.A., Howland T.J., Wei M.-H., Ibegwam C.,
RA Jalali M., Kalush F., Karpen G.H., Ke Z., Kennison J.A., Keithum K.A.,
RA Kimmel B.E., Kodira C.D., Kraft C., Kravitz S., Kulp D., Lai Z.,
RA Lasko P., Lei Y., Levitsky A.A., Li J., Li Z., Liang Y., Lin X.,
RA Liu X., Matel B., McIntosh T.C., McLeod M.P., McPherson D.,
RA Merkulov G., Milshina N.V., Mobarry C., Morris J., Moshrefi A.,
RA Mount S.M., Moy M., Murphy B., Murphy L., Muzny D.M., Nelson D.L.,
RA Nelson D.R., Nelson K.A., Nixon K., Nusskern D.R., Pacle J.M.,
RA Palazolo M., Pittman G.S., Pan S., Pollard J., Puri V., Reese M.G.,
RA Reinert K., Remington K., Saunders R.D.C., Scheeler F., Shen H.,
RA Shue B.C., Siden-Kiamos I., Simpson M., Skupski M.P., Smith T.,
RA Splier E., Spradling A.C., Stapleton M., Strong R., Sun E.,
RA Svitskas R., Tector C., Turner R., Venter E., Wang A.H., Wang X.,
RA Wang Z.-Y., Massarman D.A., Weinstein G.M., Weissbach J.,
RA Williams S.M., Woodage T., Worley K.C., Wu D., Yang S., Yao Q.A.,
RA Ye J., Yeh R.-F., Zaveri J.S., Zhan M., Zhang G., Zhao Q., Zheng L.,
RA Zheng X.H., Zhong F.N., Zhong W., Zhou X., Zhu S., Zhu X., Smith H.O.,
RA Gibbs R.A., Myers E.W., Rubin G.M., Venter J.C.;
RT "The genome sequence of Drosophila melanogaster.";
RL Science 287:2185-2195(2000).
CC -1- FUNCTION: REQUIRED FOR PROPER SIGNALING BY SEVENLESS. MAY ACT TO
CC STIMULATE THE ABILITY OF SOS TO CATALYZE RAS ACTIVATION BY
CC LINKING SEVENLESS AND SOS IN A SIGNALING COMPLEX. CAN BIND, IN
CC VITRO, TO SEVENLESS AND TO SOS.
CC -1- TISSUE SPECIFICITY: FOUND MAINLY IN THE DEVELOPING EYE AND IN THE
CC ANTENNAL DISK. ALSO OBSERVED IN OTHER IMAGINAL DISKS TESTED AND IN
CC THE EMBRYO.
CC -1- SIMILARITY: CONTAINS 1 SH2 DOMAIN.
CC -1- SIMILARITY: BELONGS TO THE GRB2 / SEM-5 / DRK FAMILY.
CC This SWISS-PROT entry is copyright. It is produced through a collaboration
CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC the European Bioinformatics Institute. There are no restrictions on its
CC use by non-profit institutions as long as its content is in no way
CC modified and this statement is not removed. Usage by and for commercial
CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>
CC or send an email to license@sib-sib.ch).
DR EMBL: L12446; AAA2898.1; -
DR EMBL: L13173; -; NOT ANNOTATED CDS.
DR EMBL: AE003818; AAF58368.1; -;

DR PIR: A46443; A46443.
DR PIR: A46444; A46444.
DR HSSP; P29354; 1GRI.
DR Flybase; FBgn0004638; drk.
DR InterPro; IPR000980; -.
DR InterPro; IPR001452; -.
DR Pfam; PF00017; SH2; 1.
DR Pfam; PF00018; SH3; 2.
DR PRINTS; PRO0452; SH2DOMAIN.
DR PROSITE; PS50001; SH2; 1.
DR PROSITE; PS50002; SH3; 2.
DR SH2 domain; SH3 domain; Transducer.
FT DOMAIN 1 58 SH3.
FT DOMAIN 60 151 SH2.
FT DOMAIN 152 211 SH3.
FT MUTAGEN 67 67 R->H: IN SU(SEV11)R1 MUTANT, OMATIDIAL
FT MUTAGEN 106 106 CELL DEVELOPMENT OBSTRUCTION.
FT H->Y: IN E(SEV)2B MUTANT, OMATIDIAL CELL
FT DEVELOPMENT OBSTRUCTION.
SQ SEQUENCE 211 AA; 24435 MM; A1D0614AF358F3C0 CRC64;
Query Match 13.6%; Score 236; DB 1; Length 211;
Best Local Similarity 29.6%; Pred. No. 2.1e-10;
Matches 56; Conservative 37; Mismatches 64; Indels 32; Gaps 5;
OY 7 NFDSESSWVGRLSGREAVALLQGGHGVFLVYRDSSTSPGIVLSVSENSRVSHYITIN 66
DB 51 NIEKKNDHWYGRITRDAEKLKSNKEGAFILRISSSGDLSVCKDQGVQHKVYL 110
OY 67 SSGPRPVPSPAPDPGSPSPRLRIGQDPDLSPLALLEFYKIHVLDYTLIEPVARSR 126
DB 111 RD-----AQSKFLVWVKFNSINELVEYHR-----TASVRSQD 144
OY 127 GSGVLRQ--EAEVYRLVFPNGNDEEDLPFKKGDLIRIDKRPEDQWMADESGRGM 184
DB 145 --VLRIMPEEMLVQALYDFVQESGELDFRRGDVITVDRSDENWNGEIG-NRKG 200
OY 185 IPVPYVERK 193
DB 201 PPAIVVTPY 209
RESULT 12
GBR2_HUMAN STANDARD: PRT: 217 AA.
AC P29354; 063057; 014450;
DT 01-DEC-1992 (Rel. 24, Created)
DT 01-DEC-1992 (Rel. 24, Last sequence update)
DT 01-OCT-2000 (Rel. 40, Last annotation update)
DE GROWTH FACTOR RECEPTOR-BOUND PROTEIN 2 (GRB2 ADAPTER PROTEIN)
DE (SH2/SH3 ADAPTER GBR2) (ASH PROTEIN).
GN GBR2 OR ASH.
OS Homo sapiens (Human), and Rattus norvegicus (Rat).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Primates; Catarrhini; Hominoidea; Homo.
OX NCBI_TaxID=9606, 10116;
RN [1]
RP SEQUENCE FROM N.A.
RC SPECIES=Human; TISSUE=Brain;
RC MEDLINE=92354060; PubMed=1322798;
RA Lowenstein E.J., Daly R.J., Batzer A.G., Li W., Margolis B.,
RA Lammer R., Ullrich A., Skolnik E.Y., Bar-Sagi D., Schlessinger J.;
RT "The SH2 and SH3 domain-containing protein GRB2 links receptor
RT tyrosine kinases to ras signaling.";
RL Cell 70:431-442(1992).
RN [2]
RP SEQUENCE FROM N.A.
RC SPECIES=Human, and Rat; TISSUE=Brain, and Lung;
RC MEDLINE=93028395; PubMed=1384039;
RA Matuoka K., Yamakawa A., Shibata M., Takenawa T.;
RT "Cloning of ASH, a ubiquitous protein composed of one Src homology
RT region (SH) 2 and two SH3 domains, from human and rat cDNA

RT libraries.";
 RL Proc. Natl. Acad. Sci. U.S.A. 89:9015-9019(1992).
 RN [3]
 RP SEQUENCE FROM N.A., AND ALTERNATIVE SPLICING.
 RC SPECIES-Rat; SPRAIN-MSTAR; TISSUE-Brain;
 RX MEDLINE-95293967; PubMed-7775438;
 RA Matanabe K., Fukuchi T., Hosoya H., Shirasawa T., Matsuoka K.,
 MIKI H., Takenawa T.;
 RT "Splicing isoforms of rat Ash/Grb2. Isolation and characterization of
 RT the cDNA and genomic DNA clones and implications for the
 RT physiological roles of the isoforms.";
 RL J. Biol. Chem. 270:13733-13739(1995).
 RN [4]
 RP SEQUENCE FROM N.A. (ISOFORM GRB3-3).
 RC SPECIES-Human; TISSUE-Placenta;
 RX MEDLINE-94233382; PubMed-8178156;
 RA Fath I., Schweighofer F., Rey I., Multon M.C., Boiziau J.,
 Duchesne M., Tocque B.;
 RT "Cloning of a Grb2 isoform with apoptotic properties.";
 RL Science 264:971-974(1994).
 RN [5]
 RP SEQUENCE FROM N.A.
 RC SPECIES-Human; TISSUE-Epidermis;
 RX MEDLINE-99162407; PubMed-10051406;
 RA Boemann H., Gehrich S., Jaross W.;
 RT "The gene structure of the human growth factor bound protein GRB2.";
 RL Genomics 56:203-207(1999).
 RN [6]
 RP ASSOCIATION WITH IRS-1.
 RX MEDLINE-93266568; PubMed-8388384;
 RA Tobe K., Matsuda K., Tamemoto H., Ueki K., Kaburagi Y., Asai S.,
 Noguchi T., Matsuda M., Tanaka S., Hattori S., Fukui Y., Akanuma Y.,
 Yazaki Y., Takenawa T., Kadowaki T.;
 RT "Insulin stimulates association of insulin receptor substrate-1 with
 RT the protein abundant Src homology/growth factor receptor-bound
 RT protein 2.";
 RL J. Biol. Chem. 268:11167-11171(1993).
 RN [7]
 RP ASSOCIATION WITH IRS-1 AND SHC.
 RX MEDLINE-93259135; PubMed-8491186;
 RA Skolnik E.Y., Lee C.-H., Batzer A., Vicentini L.M., Zhou M., Daly R.,
 Myers M.J., Jr., Backer J.M., Ullrich A., White M.F., Schlessinger J.;
 RT "The SH2/SH3 domain-containing protein GRB2 interacts with tyrosine-
 RT phosphorylated IRS1 and Shc: implications for insulin control of ras
 RT signaling.";
 RL EMBO J. 12:1929-1936(1993).
 RN [8]
 RP STRUCTURE BY NMR OF 1-56.
 RX MEDLINE-97280795; PubMed-9135122;
 RA Wittek M., Mappelli C., Lee V., Goldfarb V., Friedrichs M.S.,
 Meyers C.A., Mueller L.;
 RT "Solution structure of the Grb2 N-terminal SH3 domain complexed with
 RT a ten-residue peptide derived from SOS: direct refinement against
 RT NOESY couplings and 1H and 13C chemical shifts.";
 RL J. Mol. Biol. 267:933-952(1997).
 RN [9]
 RP STRUCTURE BY NMR OF 60-158.
 RX MEDLINE-96387228; PubMed-8794768;
 RA Thornton K.H., Mueller W.T., McConnell P., Zhu G., Saltiel A.R.,
 Thanabal V.;
 RT "Nuclear magnetic resonance solution structure of the growth factor
 RT receptor-bound protein 2 Src homology 2 domain.";
 RL Biochemistry 35:11852-11864(1996).
 RN [10]
 RP STRUCTURE BY NMR OF 53-163.
 RX Senior M.M., Frederick A.F., Black S., Perkins L.M., Wilson O.,
 Snow M.E., Wang Y.-S.;
 RT Submitted (JUN-1997) to the PDB data bank.
 RN [11]
 RP STRUCTURE BY NMR OF 159-215.
 RX MEDLINE-95187706; PubMed-7881903;
 RA Kohda D., Terasawa H., Ichikawa S., Ogura K., Hatanaka H.,
 Mandiyan V., Ullrich A., Schlessinger J., Inagaki F.;

RT "Solution structure and ligand-binding site of the carboxy-terminal
 RT SH3 domain of GRB2.";
 RL Structure 2:1029-1040(1994).
 RN [12]
 RP X-RAY CRYSTALLOGRAPHY (3.1 ANGSTROMS).
 RX MEDLINE-95232505; PubMed-7716522;
 RA Maignan S., Guilloteau J.P., Fromage N., Arnoux B., Bequart J.,
 Ducoux A.;
 RT "Crystal structure of the mammalian Grb2 adaptor.";
 RL Science 268:291-295(1995).
 RN [13]
 RP X-RAY CRYSTALLOGRAPHY (1.8 ANGSTROMS) OF 56-153.
 RX MEDLINE-98308003; PubMed-9642078;
 RA Rahuel J., Garcia-Echeveria C., Furet P., Strauss A., Caravatti G.,
 Fretz H., Schoepfer J., Gay B.;
 RT "Structural basis for the high affinity of amino-aromatic SH2
 RT phosphopeptide ligands.";
 RL J. Mol. Biol. 279:1013-1022(1998).
 RN [14]
 RP X-RAY CRYSTALLOGRAPHY (2.1 ANGSTROMS) OF 49-163.
 RX MEDLINE-99192587; PubMed-10090780;
 RA Elmayer P., France D., Gounarides J., Jarosinski M., Martin M.-S.,
 Rondeau J.-M., Sabio M., Topiol S., Weidmann B., Zurini M., Blair K.W.;
 RT "Structural and conformational requirements for high-affinity binding
 RT to the SH2 domain of Grb2(1).";
 RL J. Med. Chem. 42:971-980(1999).
 CC -!- FUNCTION: ASSOCIATES WITH ACTIVATED TYROSINE-PHOSPHORYLATED EGF
 CC RECEPTORS AND PDGF RECEPTORS VIA ITS SH2 DOMAIN. GRB2 ALSO
 CC ASSOCIATES TO OTHER CELLULAR TYROSINE-PHOSPHORYLATED PROTEINS SUCH
 CC AS IRS-1, SHC AND LNK. PROBABLY VIA THE CONCERTED ACTION OF BOTH
 CC ITS SH2 AND SH3 DOMAINS. IT ALSO SEEMS TO INTERACT WITH RAS
 CC IN THE SIGNALING PATHWAY LEADING TO DNA SYNTHESIS. BINDS TO AND
 CC TRANSLOCATES THE GUANINE NUCLEOTIDE EXCHANGE FACTORS SOS.
 CC -!- FUNCTION: PROBABLY REPRESENTS A REGULATORY SUBUNIT OF DOWNSTREAM
 CC SIGNALING MOLECULES WHOSE ACTIVITY IS MODULATED BY RECEPTOR
 CC BINDING. A 55 KDA PHOSPHOPROTEIN OF UNKNOWN FUNCTION WHICH BINDS
 CC TO GRB2 IN RESPONSE TO GROWTH FACTOR STIMULATION COULD BE A
 CC DOWNSTREAM SIGNALING MOLECULE CANDIDATE.
 CC -!- FUNCTION: ISOFORM GRB3-3 DOES NOT BIND TO PHOSPHORYLATED EPIDERMAL
 CC GROWTH FACTOR RECEPTOR (EGFR) BUT INHIBITS EGF-INDUCED
 CC TRANSACTIVATION OF A RAS-RESPONSIVE ELEMENT. GRB3-3 ACTS AS A
 CC DOMINANT NEGATIVE PROTEIN OVER GRB2 AND BY SUPPRESSING
 CC PROLIFERATIVE SIGNALS, MAY TRIGGER ACTIVE PROGRAMMED CELL DEATH.
 CC -!- ALTERNATIVE PRODUCTS: A NUMBER OF FORMS ARE PRODUCED BY
 CC ALTERNATIVE SPLICING.
 CC -!- TISSUE SPECIFICITY: WIDE TISSUE AND CELL DISTRIBUTION.
 CC -!- SIMILARITY: CONTAINS 1 SH2 DOMAIN.
 CC -!- SIMILARITY: CONTAINS 2 SH3 DOMAINS.
 CC -!- SIMILARITY: BELONGS TO THE GRB2 / SEM-5 / DRK FAMILY.
 CC -----
 CC This SWISS-PROT entry is copyright. It is produced through a collaboration
 CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
 CC the European Bioinformatics Institute. There are no restrictions on its
 CC use by non-profit institutions as long as its content is in no way
 CC modified and this statement is not removed. Usage by and for commercial
 CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>
 CC or send an email to license@sib-sib.ch).
 CC -----
 DR EMBL: M96995; AAA58448.1; -;
 DR EMBL: X62852; CAA44664.1; -;
 DR EMBL: X62853; CAA44665.1; -;
 DR EMBL: D49846; BAA08645.1; -;
 DR EMBL: L29511; AAC37549.1; -;
 DR EMBL: AF063618; AAC72075.1; -;
 DR EMBL: AF063614; AAC72075.1; JOINED.
 DR EMBL: AF063615; AAC72075.1; JOINED.
 DR EMBL: AF063616; AAC72075.1; JOINED.
 DR EMBL: AF063617; AAC72075.1; JOINED.
 DR PIR: A43321; A43321.
 DR PIR: S26050; S26050.
 DR PDB: 1GRI; 08-MAR-96.
 DR PDB: 1GFC; 31-AUG-94.
 DR PDB: 1GFD; 31-AUG-94.

```
DR PDB; 1GHU; 27-JAN-97.
DR PDB; 1TZE; 07-JUL-97.
DR PDB; 1FHS; 17-JUN-98.
DR PDB; 1BM2; 05-AUG-98.
DR PDB; 1BMB; 29-JUL-98.
DR PDB; 1ZEP; 30-MAR-99.
DR MIM; 108355; -.
DR InterPro: IPR000980; -.
DR InterPro: IPR001452; -.
DR Pfam; PF00017; SH2; 1.
DR Pfam; PF00018; SH3; 2.
DR PRINTS; PR00401; SH2DOMAIN.
DR PRINTS; PR00452; SH3DOMAIN.
DR PROSITE; PS50001; SH2; 1.
DR PROSITE; PS50002; SH3; 2.
KW SH2 domain; SH3 domain; Alternative splicing; 3D-structure.
FT DOMAIN 1 58 SH3.
FT DOMAIN 60 152 SH2.
FT VARSPLIC 156 215 SH3.
FT VARSPLIC 60 100 MISSING (IN ISOFORM GRB3-3).
FT VARSPLIC 157 170 MISSING (IN ISOFORM ASH-M).
FT MUTAGEN 49 49 P->L: INEFFECTIVE IN DNA SYNTHESIS.
FT MUTAGEN 203 203 G->R: INEFFECTIVE IN DNA SYNTHESIS.
SQ SEQUENCE 217 AA; 25206 MW; 83A4B0BA1B24BDC4 CRC64;

Query Match 12.9%; Score 224; DB 1; Length 217;
Best Local Similarity 27.9%; Pred. No. 1.6e-09;
Matches 53; Conservative 44; Mismatches 57; Indels 36; Gaps 7;

QY 7 NFDSESSWYMGRLSROEAVALLQGORH-GVFLVRSSTSPGQDYLVSVSENSRVSHYII 65
DB 51 NYEMKPHMWFECFKIDRAAEMLSKQRDGAFLIHESSEAPGDFSLVKFENDVQHFV 110
QY 66 NSGPRPPPPSAOPPPGVSPRLIGDQEDSLPALLEFKIHLDTTLLIEPYARSR 125
DB 111 LRDG-----AGKTYLWYKFNLSLNEIYDHR-----STG-----VSRNQ 144
QY 126 QGSGVILRQ-----EEAEYVRLAFDENGDEDLPPKKGDIIRIRKPPEOMNADSSG 180
DB 145 Q---ILRLDIEVPPQPTVYQALFDLPDQDEGLGRFRDFTIHVMDNSDPNMWKKGA-CHG 200
QY 181 KRGMIPVPY 190
DB 201 QTGMPPRNVY 210

RESULT 13
GRB2_MOUSE STANDARD; PRT; 217 AA.
ID GRB2_MOUSE 060631; 061240;
DT 01-NOV-1997 (Rel. 35, Created)
DT 01-NOV-1997 (Rel. 35, Last sequence update)
DT 15-JUL-1999 (Rel. 38, Last annotation update)
DE GROWTH FACTOR RECEPTOR-BOUND PROTEIN 2 (GRB2 ADAPTER PROTEIN)
DE (SH2/SH3 ADAPTER GRB2).
GN GRB2.
OS Mus musculus (Mouse).
OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX NCBI_TaxId=10090;
RN [1]
RP SEQUENCE FROM N.A.
RC STRAIN=BAIB/C.
RA MEDLINE=93360985; PubMed=7689150;
RA Suen K., Bustelo X.R., Pawson T., Barbacid M.;
RT "Molecular cloning of the mouse grb2 gene: differential interaction
RT of the Grb2 adaptor protein with epidermal growth factor and nerve
RT growth factor receptors."
RL Mol. Cell. Biol. 13:5500-5512(1993).
RN [2]
RC SEQUENCE FROM N.A. (ISOFORM GRB3-3).
RP STRAIN=BAIB/C;
```

```
RA Tanaka S.;
RL Submitted (JUN-1996) to the EMBL/GenBank/DBJ databases.
RN [3]
RP STRUCTURE BY NMR OF 1-59.
RX MEDLINE=97280795; PubMed=9135122;
RX Wittekand M., Mepeell C., Lee V., Goldfarb V., Friedrichs M.S.,
RA Meyers C.A., Mueller L.;
RT "Solution structure of the Grb2 N-terminal SH3 domain complexed with
RT a ten-residue peptide derived from SOS: direct refinement against
RT NOES, J-couplings and 1H and 13C chemical shifts."
RL J. Mol. Biol. 267:933-952(1997).
CC -1- FUNCTION: ASSOCIATES WITH ACTIVATED TYROSINE-PHOSPHORYLATED EGF
CC RECEPTORS AND PDGF RECEPTORS VIA ITS SH2 DOMAIN. GRB2 ALSO
CC ASSOCIATES TO OTHER CELLULAR TYROSINE-PHOSPHORYLATED PROTEINS SUCH
CC AS IRS-1, SHC AND LNK: PROBABLY VIA THE CONCERTED ACTION OF BOTH
CC ITS SH2 AND SH3 DOMAINS. IT ALSO SEEMS TO INTERACT WITH RAS
CC IN THE SIGNALING PATHWAY LEADING TO DNA SYNTHESIS. BINDS TO AND
CC TRANSLOCATES THE GUANINE NUCLEOTIDE EXCHANGE FACTORS SOS.
CC -1- FUNCTION: PROBABLY REPRESENTS A REGULATORY SUBUNIT OF DOWNSTREAM
CC SIGNALING MOLECULES WHOSE ACTIVITY IS MODULATED BY RECEPTOR
CC BINDING. A 55 KDA PHOSPHOPROTEIN OF UNKNOWN FUNCTION WHICH BINDS
CC TO GRB2 IN RESPONSE TO GROWTH FACTOR STIMULATION COULD BE A
CC DOWNSTREAM SIGNALING MOLECULE CANDIDATE.
CC -1- FUNCTION: ISOFORM GRB3-3 DOES NOT BIND TO PHOSPHORYLATED EPIDERMAL
CC GROWTH FACTOR RECEPTOR (EGFR) BUT INHIBITS EGF-INDUCED
CC TRANSACTIVATION OF A RAS-RESPONSIVE ELEMENT. GRB3-3 ACTS AS A
CC DOMINANT NEGATIVE PROTEIN OVER GRB2 AND BY SUPPRESSING
CC PROLIFERATIVE SIGNALS, MAY TRIGGER ACTIVE PROGRAMMED CELL DEATH
CC (BY SIMILARITY).
CC -1- ALTERNATIVE PRODUCTS: A NUMBER OF FORMS ARE PRODUCED BY
CC ALTERNATIVE SPLICING.
CC -1- SIMILARITY: CONTAINS 1 SH2 DOMAIN.
CC -1- SIMILARITY: CONTAINS 2 SH3 DOMAINS.
CC -1- SIMILARITY: BELONGS TO THE GRB2 / SEM-5 / DRK FAMILY.
CC
CC THIS SWISS-PROT entry is copyright. It is produced through a collaboration
CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC the European Bioinformatics Institute. There are no restrictions on its
CC use by non-profit institutions as long as its content is in no way
CC modified and this statement is not removed. Usage by and for commercial
CC entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC or send an email to license@isb-sib.ch).
CC
DR EMBL; U07617; AAB40022.1; -.
DR EMBL; D85748; BAA12862.1; -.
DR PDB; 1GBQ; 04-SEP-97.
DR PDB; 2GBQ; 04-SEP-97.
DR PDB; 3GBQ; 04-SEP-97.
DR PDB; 4GBQ; 04-SEP-97.
DR PDB; 1GBR; 26-JAN-95.
DR MGD; MGI:95805; Grb2.
DR InterPro: IPR000980; -.
DR InterPro: IPR001452; -.
DR Pfam; PF00017; SH2; 1.
DR Pfam; PF00018; SH3; 2.
DR PRINTS; PR00401; SH2DOMAIN.
DR PRINTS; PR00452; SH3DOMAIN.
DR PROSITE; PS50001; SH2; 1.
DR PROSITE; PS50002; SH3; 2.
KW SH2 domain; SH3 domain; Alternative splicing; 3D-structure.
FT DOMAIN 1 58 SH3.
FT DOMAIN 60 152 SH2.
FT VARSPLIC 156 215 SH3.
FT VARSPLIC 60 100 MISSING (IN ISOFORM GRB3-3).
SQ SEQUENCE 217 AA; 25238 MW; 97F4A4FE4B248DDE CRC64;

Query Match 12.9%; Score 224; DB 1; Length 217;
Best Local Similarity 27.9%; Pred. No. 1.6e-09;
Matches 53; Conservative 44; Mismatches 57; Indels 36; Gaps 7;

QY 7 NFDSESSWYMGRLSROEAVALLQGORH-GVFLVRSSTSPGQDYLVSVSENSRVSHYII 65
DB 51 NYEMKPHMWFECFKIDRAAEMLSKQRDGAFLIHESSEAPGDFSLVKFENDVQHFV 110
QY 66 NSGPRPPPPSAOPPPGVSPRLIGDQEDSLPALLEFKIHLDTTLLIEPYARSR 125
DB 111 LRDG-----AGKTYLWYKFNLSLNEIYDHR-----STG-----VSRNQ 144
QY 126 QGSGVILRQ-----EEAEYVRLAFDENGDEDLPPKKGDIIRIRKPPEOMNADSSG 180
DB 145 Q---ILRLDIEVPPQPTVYQALFDLPDQDEGLGRFRDFTIHVMDNSDPNMWKKGA-CHG 200
QY 181 KRGMIPVPY 190
DB 201 QTGMPPRNVY 210
```

Db 51 NYTEMKPHWFECKIPRAKAEMLSKQRHDAFLIRESESAAGDPSLSVKGNVQHFV 110
 QY 66 NSSGPRPVPPSPADPPGVSPSRLRIGDQFDSLPALEFFKHYLDTTLIEPVARS 125
 Db 111 LRGC-----AGKYFLWVVKNSINLELVYHR-----STS-----VSRNQ 144
 QY 126 QGSGVILRO-----EEAEVYRALFPDNGNDEEDLPFKKGDILIRDKPEEGMNAEDSEG 180
 Db 145 Q---IFLRDIEQYPPQPTVQALFPDPEDEGLGFRGDFTLVNDSDPMWKA-CHG 200
 QY 181 KRGMIFFPVY 190
 Db 201 QTGMFPRNVY 210

RESULT 14
 GRB2_CHICK STANDARD; PRT; 217 AA.
 ID GRB2_CHICK
 AC 007883;
 DT 01-FEB-1995 (Rel. 31, Last sequence update)
 DT 01-FEB-1995 (Rel. 31, Last sequence update)
 DT 15-JUL-1999 (Rel. 38, Last annotation update)
 DE GROWTH FACTOR RECEPTOR-BOUND PROTEIN 2 (GRB2 ADAPTER PROTEIN)
 DE (SH2/SH3 ADAPTER GRB2) (ASH PROTEIN).
 GN GRB2.
 OS Gallus gallus (Chicken).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;
 OC Gallus.
 OX NCBI_TaxID=9031;
 RN (1)
 RP SEQUENCE FROM N.A.
 RC TISSUE=Brain;
 RX MEDLINE=94085795; PubMed=8262390;
 RA Masenius V.-M., Merilainen J., Lehto V.-P.;
 RT *Sequence of a chicken cDNA encoding a GRB2 protein.*;
 RL Gene 134:299-300(1993).
 CC -1- FUNCTION: ASSOCIATES WITH ACTIVATED TYROSINE-PHOSPHORYLATED EGF
 RECEPTORS AND PDGF RECEPTORS VIA ITS SH2 DOMAIN. GRB2 ALSO
 CC ASSOCIATES TO OTHER CELLULAR TYROSINE-PHOSPHORYLATED PROTEINS SUCH
 CC AS IRS-1, SHC AND LNK; PROBABLY VIA THE CONCERTED ACTION OF BOTH
 CC ITS SH2 AND SH3 DOMAINS. IT ALSO SEEMS TO INTERACT WITH RAS
 CC IN THE SIGNALING PATHWAY LEADING TO DNA SYNTHESIS. BINDS TO AND
 CC TRANSLOCATES THE GUANINE NUCLEOTIDE EXCHANGE FACTORS SOS.
 CC -1- FUNCTION: PROBABLY REPRESENTS A REGULATORY SUBUNIT OF DOWNSTREAM
 CC SIGNALING MOLECULES WHOSE ACTIVITY IS MODULATED BY RECEPTOR
 CC BINDING. A 55 KDA PHOSPHOPROTEIN OF UNKNOWN FUNCTION WHICH BINDS
 CC TO GRB2 IN RESPONSE TO GROWTH FACTOR STIMULATION COULD BE A
 CC DOWNSTREAM SIGNALING MOLECULE CANDIDATE.
 CC -1- TISSUE SPECIFICITY: WIDE TISSUE AND CELL DISTRIBUTION.
 CC -1- SIMILARITY: CONTAINS 1 SH2 DOMAIN.
 CC -1- SIMILARITY: CONTAINS 2 SH3 DOMAINS.
 CC -1- SIMILARITY: BELONGS TO THE GRB2 / SEM-5 / DRK FAMILY.
 CC
 CC This SWISS-PROT entry is copyright. It is produced through a collaboration
 CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
 CC the European Bioinformatics Institute. There are no restrictions on its
 CC use by non-profit institutions as long as its content is in no way
 CC modified and this statement is not removed. Usage by and for commercial
 CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>
 CC or send an email to license@isb-sib.ch).
 CC
 CC EMBL: LI9258; AAA16318.1;
 DR PIR: J70664; J70664.
 DR HSSP: P29354; 1GRI.
 DR InterPro: IPR0000980;
 DR InterPro: IPR001452;
 DR Pfam: PF00017; SH2; 1.
 DR Pfam: PF00018; SH3; 2.
 DR PRINTS: PR00452; SH3DOMAIN.
 DR PROSITE: PS50001; SH2; 1.
 DR PROSITE: PS50002; SH3; 2.
 KM SH2 domain; SH3 domain.

FT DOMAIN 1 58 SH3.
 FT DOMAIN 60 152 SH2.
 FT DOMAIN 156 215 SH3.
 SQ SEQUENCE 217 AA; 25076 MW; DDC9A84ECD52859 CRC64;

Query Match 12.6%; Score 218; DB 1; Length 217;
 Best Local Similarity 27.9%; Pred. No. 4.2e-09;
 Matches 53; Conservative 44; Mismatches 57; Indels 36; Gaps 7;

QY 7 NFDSEERSWYMGRLSGROEVALLOGORH-GVELYRDSSTSGPVYLSVNSRSHYII 65
 Db 51 NYTEMKPHWFECKIPRAKAEMLSKQRHDAFLIRESESAAGDPSLSVKGNVQHFV 110
 QY 66 NSSGPRPVPPSPADPPGVSPSRLRIGDQFDSLPALEFFKHYLDTTLIEPVARS 125
 Db 111 LRGC-----AGKYFLWVVKNSINLELVYHR-----STS-----VSRNQ 144
 QY 126 QGSGVILRO-----EEAEVYRALFPDNGNDEEDLPFKKGDILIRDKPEEGMNAEDSEG 180
 Db 145 Q---IFLRDIEQYPPQPTVQALFPDPEDEGLGFRGDFTLVNDSDPMWKA-CHG 200
 QY 181 KRGMIFFPVY 190
 Db 201 QTGMFPRNVY 210

RESULT 15
 GRB2_XENIA STANDARD; PRT; 217 AA.
 ID GRB2_XENIA
 AC P87379;
 DT 15-DEC-1998 (Rel. 37, Created)
 DT 15-DEC-1998 (Rel. 37, Last sequence update)
 DT 15-JUL-1999 (Rel. 38, Last annotation update)
 DE GROWTH FACTOR RECEPTOR-BOUND PROTEIN 2 (GRB2 ADAPTER PROTEIN)
 DE (SH2/SH3 ADAPTER GRB2).
 GN GRB2.
 OS Xenopus laevis (African clawed frog).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Amphibia; Batrachia; Anura; Mesobatrachia; Pipidoidea; Pipidae;
 OC Xenopodinae; Xenopus.
 OX NCBI_TaxID=6355;
 RN (1)
 RP SEQUENCE FROM N.A.
 RA Lu W., Mayer B.J.;
 RL Submitted (Feb-1997) to the EMBL/Genbank/DBJ databases.
 CC -1- FUNCTION: ASSOCIATES WITH ACTIVATED TYROSINE-PHOSPHORYLATED EGF
 RECEPTORS AND PDGF RECEPTORS VIA ITS SH2 DOMAIN. GRB2 ALSO
 CC ASSOCIATES TO OTHER CELLULAR TYROSINE-PHOSPHORYLATED PROTEINS SUCH
 CC AS IRS-1, SHC AND LNK; PROBABLY VIA THE CONCERTED ACTION OF BOTH
 CC ITS SH2 AND SH3 DOMAINS. IT ALSO SEEMS TO INTERACT WITH RAS
 CC IN THE SIGNALING PATHWAY LEADING TO DNA SYNTHESIS (BY
 CC PROTEINS IN THE SIGNALING PATHWAY LEADING TO DNA SYNTHESIS (BY
 CC SIMILARITY).
 CC -1- FUNCTION: PROBABLY REPRESENTS A REGULATORY SUBUNIT OF DOWNSTREAM
 CC SIGNALING MOLECULES WHOSE ACTIVITY IS MODULATED BY RECEPTOR
 CC BINDING. A 55 KDA PHOSPHOPROTEIN OF UNKNOWN FUNCTION WHICH BINDS
 CC TO GRB2 IN RESPONSE TO GROWTH FACTOR STIMULATION COULD BE A
 CC DOWNSTREAM SIGNALING MOLECULE CANDIDATE (BY SIMILARITY).
 CC -1- SIMILARITY: CONTAINS 1 SH2 DOMAIN.
 CC -1- SIMILARITY: CONTAINS 2 SH3 DOMAINS.
 CC -1- SIMILARITY: BELONGS TO THE GRB2 / SEM-5 / DRK FAMILY.
 CC
 CC This SWISS-PROT entry is copyright. It is produced through a collaboration
 CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
 CC the European Bioinformatics Institute. There are no restrictions on its
 CC use by non-profit institutions as long as its content is in no way
 CC modified and this statement is not removed. Usage by and for commercial
 CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>
 CC or send an email to license@isb-sib.ch).
 CC
 CC EMBL: U89775; AAB49699.1;
 DR InterPro: IPR000980;
 DR InterPro: IPR001452;

